

REMARKS

I. General

Claims 1-44 are pending in the present application. The issues outstanding with respect to the present Office Action are as follows:

- Claims 1-10, 13, and 18-22 have been rejected under 35 U.S.C. §102(b) as anticipated by *Nicholson et al.*, Clin. Exp. Pharmacol. Physiol. 1993; 20: 535-540 (hereinafter “*Nicholson*”).
- Claims 1, 9, and 10 have been rejected under 35 U.S.C. §103(a) as unpatentable over *Nicholson* and further in view of *Tavel et al.*, Chest 2001; 119: 907-925 (hereinafter “*Tavel*”).
- Claims 1, and 15-17 have been rejected under 35 U.S.C. §103(a) as being unpatentable over *Nicholson* and further in view of *Raza et al.*, Int. J. Cardio. 2001; 31: 157-167 (hereinafter “*Raza*”).
- Claims 1-9, 11, 12, 14, 18-32, 34, 36 and 40-44 have been rejected under 35 U.S.C. §103(a) as unpatentable over *Marumoto et al.*, Clinical Science 1995; 88: 551-556 (hereinafter “*Marumoto*”).
- Claims 1, 9, 10, 23, 31, 32, 33, and 35 have been rejected under 35 U.S.C. §103(a) as being unpatentable over *Marumoto* and further in view of *Tavel*.
- Claims 1, 15-17, 23 and 37-39 have been rejected under 35 U.S.C. §103(a) as being unpatentable over *Marumoto* and further in view of *Raza*.

Applicant respectfully traverses the outstanding rejections and requests reconsideration and withdrawal thereof in light of the remarks contained herein.

II. Issues Under 35 U.S.C. § 102(b)

Claim 1 and its dependent claims 2-10, 13, and 18-22 stand rejected under 35 U.S.C. §102(b) as anticipated over *Nicholson*. To anticipate a claim under 35 U.S.C. § 102, a

reference must teach every element of the claim, see M.P.E.P. § 2131. The applied reference does not teach every element of the claims. Accordingly, Applicant respectfully traverses the rejection.

A. **Independent Claim 1**

Claim 1 recites “**calculating a relative change** in the marker related to the BNP level.” The “relative change in BNP level” is defined as “the change in the BNP level immediately after exercise as compared to the baseline level,” see spec [0050]. Examples are given. A “baseline BNP” level is defined as “the BNP level before a specific event,” for example, “the BNP level after exercise is compared to a baseline BNP level before exercise,” see [0050]. On page 11 of the Action, the Examiner states that *Nicholson* teaches “. . . calculating the relative change in BNP measurements at different time points . . .” in the section under Study Protocol and Figure 1 on page 537 of *Nicholson*.” Applicant asserts this is a wholly inaccurate statement. The section under Study Protocol teaches that blood samples taken from subjects immediately before exercise, 6 minutes after the start of exercise, completion of exercise, and 10, 20, and 30 minutes after exercise completion were tested for BNP levels. Figure 1 plots mean BNP levels of patients with ischaemic heart disease immediately before exercise, at completion of exercise, and 10, 20, and 30 minutes after exercise completion. Applicant asserts that *Nicholson* does not teach **calculating a change** in BNP level (a marker related to BNP). As such, Applicant asserts that *Nicholson* does not teach **calculating a relative change** in BNP level (a marker related to BNP) as described in paragraph [0050] and Examples 6 and 7, and illustrated in Table 1.

Additionally, claim 1 recites the limitation “wherein coronary artery disease is detected in said mammal if the **relative change** in marker related to BNP after cardiac stress is greater than a predetermined clinically effective threshold value.” On page 11 of the Action, the Examiner states that since “Applicants do not define the predetermined clinically effective threshold value in the specification as a number, . . . thus the resting BNP levels recorded in *Nicholson et al.* could serve as a threshold value.” The term “clinically effective threshold value” is discussed in paragraphs [0053] through [0057] of Applicant’s specification. Paragraph [0057] clearly states that “clinically effective threshold value” refers to **relative changes** in BNP levels with a predetermined threshold value correctly indicating

the presence or absence of the disease, condition, or syndrome. Applicant would like to point out that resting BNP levels in *Nicholson* are values corresponding to BNP levels at a point in time, before exercise, and are not values corresponding to a **change** in BNP levels, much less to a **relative change** in BNP levels. Accordingly, Applicant asserts that resting BNP levels recorded in *Nicholson* could not serve as a threshold value.

Even assuming arguendo, Applicant would like to point out that in *Nicholson* coronary heart disease is not detected in a mammal if the change in marker related to BNP after cardiac stress is greater than a predetermined clinically effective threshold value if the predetermined clinically effective threshold value is taken as the resting BNP levels. Looking at plasma BNP basal (resting BNP levels) and BNP peak (BNP levels at exercise completion) for patients 1-16 in Table 1, one could assume that the values imply a change in BNP levels, for example, patient 1 would have a change in BNP level of 8. If the clinically effective threshold value is taken as 27, the resting BNP level for patient 1, patient 1 would not be considered to suffer from coronary heart disease since 8 is less than 27. The same analysis applies to patients 2-16. This method would not detect coronary heart disease in patients 1-16. Furthermore, as stated above, *Nicholson* teaches measuring BNP levels and does not teach **calculating a change** in BNP levels, much less calculating a **relative change** in BNP levels.

Because all the claim limitations are not met by *Nicholson*, Applicant respectfully requests withdrawal of the rejection.

B. Dependent Claims 2-10, 13, and 18-22

Claims 2-10, 13, and 18-22 depend from claim 1. Accordingly, each of these dependent claims is asserted to be patentable over the 35 U.S.C. § 102 rejections of record at least for the reasons set forth above with respect to claim 1.

III. Issues Under 35 U.S.C. § 103(a)

To render a claim unpatentable under 35 U.S.C. § 103, all the claim limitations must be taught or suggested by the prior art, M.P.E.P. § 2143.03. Additionally, if an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious,

see M.P.E.P. § 2143.03. The 35 U.S.C. § 103 rejections on record do not meet the foregoing criteria. Accordingly, Applicant respectfully traverses these rejections.

A. The 35 U.S.C. § 103 Rejections Based Upon *Nicholson*

1. Rejections Based Upon *Nicholson* in view of *Tavel*

Claims 1, 9, and 10 stand rejected under 35 U.S.C. §103(a) as unpatentable over *Nicholson* and further in view of *Tavel*. As discussed above, *Nicholson* does not meet the claim limitations of claim 1. Applicant has not been able to identify the limitations absent from *Nicholson* in the disclosure of *Tavel*, and the Examiner has not shown otherwise. Because these claim limitations are not taught or suggested by *Nicholson* nor *Nicholson* in view of *Tavel*, the 35 U.S.C. § 103 rejection of claim 1 fails. Applicant respectfully requests withdrawal of the rejection.

Claims 9 and 10 are dependent on claim 1 and include all of the limitations of claim 1. Because these claim limitations are not met by *Nicholson* nor *Nicholson* in view of *Tavel*, the 35 U.S.C. § 103 rejections of claims 9 and 10 fail. Applicant respectfully requests withdrawal of the rejections.

2. Rejections Based Upon *Nicholson* in view of *Raza*

Claims 1, and 15-17 stand rejected under 35 U.S.C. §103(a) as being unpatentable over *Nicholson* and further in view of *Raza*. As discussed above, *Nicholson* does not meet the claim limitations of claim 1. Applicant has not been able to identify the limitations absent from *Nicholson* in the disclosure of *Raza*, and the Examiner has not shown otherwise. Because these claim limitations are not taught or suggested by *Nicholson* nor *Nicholson* in view of *Raza*, the 35 U.S.C. § 103 rejection of claim 1 fails. Applicant respectfully requests withdrawal of the rejection.

Claims 15-17 are dependent on claim 1 and include all of the limitations of claim 1. Because these claim limitations are not met by *Nicholson* nor *Nicholson* in view of *Raza*, the 35 U.S.C. § 103 rejections of claims 15-17 fail. Applicant respectfully requests withdrawal of the rejections.

B. The 35 U.S.C. § 103 Rejections Based Upon *Marumoto*

1. Rejections Based Upon *Marumoto*

Claims 1-9, 11, 12, 14, 18-32, 34, 36 and 40-44 stand rejected under 35 U.S.C. §103(a) as unpatentable over *Marumoto*. Applicant respectfully traverses the rejection.

a. Independent Claim 1

Claim 1 recites “**calculating a relative change** in the marker related to the BNP level.” The “relative change in BNP level” is defined as “the change in the BNP level immediately after exercise as compared to the baseline level,” see spec [0050]. Examples are given. A “baseline BNP” level is defined as “the BNP level before a specific event,” for example, “the BNP level after exercise is compared to a baseline BNP level before exercise,” see [0050]. On page 4 of the Action, the Examiner states that “Figure 2 of *Marumoto* clearly suggests that taking BNP levels any time from peak exercise to 30 minutes post-exercise would show a difference in BNP levels between healthy and heart diseased patients” Applicant asserts this is a wholly inaccurate statement. Figure 2 plots BNP levels at rest, peak exercise and 30 minutes after exercise. Even if it would have been obvious to measure BNP levels at any time from peak exercise to 30 minutes post-exercise and plot this number in Figure 2, the claim limitation at hand would still not be met. Measuring BNP levels at a time post-cardiac stress does not render obvious **calculating a relative change** in BNP. Applicant asserts that *Marumoto* neither teaches nor suggests **calculating a change** in BNP level. As such, Applicant asserts that Nicholson neither teaches nor suggests **calculating a relative change** in BNP level (a marker related to BNP) as described in paragraph [0050] and Examples 6 and 7, and illustrated in Table 1.

Additionally, claim 1 recites the limitation “wherein coronary artery disease is detected in said mammal if the **relative change** in marker related to BNP after cardiac stress is greater than a predetermined clinically effective threshold value.” On page 4 of the Action, the Examiner states that since “Applicants do not define the predetermined clinically effective threshold value in the specification as a number, . . . thus the resting BNP levels recorded in Nicholson et al. could serve as a threshold value.” The term “clinically effective threshold value” is discussed in paragraphs [0053] through [0057] of Applicant’s

specification. Paragraph [0057] clearly states that “clinically effective threshold value” refers to **relative changes** in BNP levels with a predetermined threshold value correctly indicating the presence or absence of the disease, condition, or syndrome. Applicant would like to point out that resting BNP levels in *Marumoto* are values corresponding to BNP levels at a point in time, before exercise, and are not values corresponding to a **change** in BNP levels, much less to a **relative change** in BNP levels. Accordingly, Applicant asserts that resting BNP levels recorded in *Marumoto* could not serve as a threshold value.

Because all the claim limitations are not met by *Marumoto*, Applicant respectfully requests withdrawal of the rejection.

b. Dependent Claims 2-9, 11, 12, 14, and 18-22

Claims 2-9, 11, 12, 14, and 18-22 are dependent on claim 1 and include all of the limitations of claim 1. Because these claim limitations are not met by *Marumoto*, the 35 U.S.C. § 103 rejections of claims 2-9, 11, 12, 14, and 18-22 fail. Applicant respectfully requests withdrawal of the rejections.

c. Independent Claim 23

Claim 23 recites “calculating a **relative change** in the marker related to the BNP level.” The “relative change in BNP level” is defined as “the change in the BNP level immediately after exercise as compared to the baseline level,” see spec [0050]. Examples are given. A “baseline BNP” level is defined as “the BNP level before a specific event,” for example, “the BNP level after exercise is compared to a baseline BNP level before exercise,” see [0050]. On page 4 of the Action, the Examiner states that “Figure 2 of *Marumoto* clearly suggests that taking BNP levels any time from peak exercise to 30 minutes post-exercise would show a difference in BNP levels between healthy and heart diseased patients” Applicant asserts this is a wholly inaccurate statement. Figure 2 plots BNP levels at rest, peak exercise and 30 minutes after exercise. Even if it would have been obvious to measure BNP levels at any time from peak exercise to 30 minutes post-exercise and plot this number in Figure 2, the claim limitation at hand would still not be met. Measuring BNP levels at a time post-cardiac stress does not render obvious **calculating a relative change** in BNP. Applicant asserts that *Marumoto* neither teaches nor suggests **calculating a change** in BNP

level. As such, Applicant asserts that Nicholson neither teaches nor suggests **calculating a relative change** in BNP level (a marker related to BNP) as described in paragraph [0050] and Examples 6 and 7, and illustrated in Table 1.

Additionally, claim 23 recites the limitations “wherein the **relative change** in the marker related to BNP level correlates with severity of coronary artery disease . . . ” and “wherein the higher the relative change, the greater the severity of coronary artery disease.” On page 4 of the Action, the Examiner states that since “Applicants do not define the predetermined clinically effective threshold value in the specification as a number, . . . thus the resting BNP levels recorded in Nicholson et al. could serve as a threshold value.” The term “clinically effective threshold value” is discussed in paragraphs [0053] through [0057] of Applicant’s specification. Paragraph [0057] clearly states that “clinically effective threshold value” refers to **relative changes** in BNP levels with a predetermined threshold value correctly indicating the presence or absence of the disease, condition, or syndrome. Applicant would like to point out that resting BNP levels in *Marumoto* are values corresponding to BNP levels at a point in time, before exercise, and are not values corresponding to a **change** in BNP levels, much less a **relative change** in BNP levels. Accordingly, Applicant asserts that resting BNP levels recorded in *Marumoto* could not serve as a threshold value.

Because all the claim limitations are not met by *Marumoto*, Applicant respectfully requests withdrawal of the rejection.

d. Dependent Claims 24-32, 34, 36 and 40-44

Claims 24-32, 34, 36 and 40-44 are dependent on claim 1 and include all of the limitations of claim 1. Because these claim limitations are not met by *Marumoto*, the 35 U.S.C. § 103 rejections of claims 24-32, 34, 36 and 40-44 fail. Applicant respectfully requests withdrawal of the rejections.

2. Rejections Based Upon *Marumoto* in view of *Tavel*

Claims 1, 9, 10, 23, 31, 32, 33, and 35 stand rejected under 35 U.S.C. §103(a) as unpatentable over *Marumoto* and further in view of *Tavel*. Applicant respectfully traverses the rejection.

As discussed above, *Marumoto* does not meet the claim limitations of claims 1 and 23. Applicant has not been able to identify the limitations absent from *Marumoto* in the disclosure of *Tavel*, and the Examiner has not shown otherwise. Because these claim limitations are not taught or suggested by *Marumoto* nor *Marumoto* in view of *Tavel*, the 35 U.S.C. § 103 rejections of claims 1 and 23 fail. Applicant respectfully requests withdrawal of the rejections.

Claims 9 and 10 are dependent on claim 1 and include all of the limitations of claim 1. Claims 31-33 are dependent on claim 23 and include all of the limitations of claim 23. Applicant has not been able to identify the limitations absent from *Marumoto* in the disclosure of *Tavel*, and the Examiner has not shown otherwise. Because these claim limitations are not taught or suggested by *Marumoto* nor *Marumoto* in view of *Tavel*, the 35 U.S.C. § 103 rejections of claims 9, 10, and 31-33 fail. Applicant respectfully requests withdrawal of the rejections.

3. Rejections Based Upon *Marumoto* in view of *Raza*

Claims 1, 15-17, 23 and 37-39 stand rejected under 35 U.S.C. §103(a) as being unpatentable over *Marumoto* and further in view of *Raza*. Applicant respectfully traverses the rejection.

As discussed above, *Marumoto* does not meet the claim limitations of claims 1 and 23. Applicant has not been able to identify the limitations absent from *Marumoto* in the disclosure of *Raza*, and the Examiner has not shown otherwise. Because these claim limitations are not taught or suggested by *Marumoto* nor *Marumoto* in view of *Raza*, the 35 U.S.C. § 103 rejections of claims 1 and 23 fail. Applicant respectfully requests withdrawal of the rejections.

Claims 15-17 are dependent on claim 1 and include all of the limitations of claim 1. Claims 37-39 are dependent on claim 23 and include all of the limitations of claim 23. Applicant has not been able to identify the limitations absent from *Marumoto* in the disclosure of *Raza*, and the Examiner has not shown otherwise. Because these claim limitations are not taught or suggested by *Marumoto* nor *Marumoto* in view of *Raza*, the 35 U.S.C. § 103 rejections of claims 15-17 and 37-39 fail. Applicant respectfully requests withdrawal of the rejections.

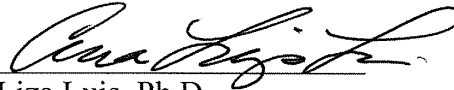
IV. Conclusion

In view of the above, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P02680US1 from which the undersigned is authorized to draw.

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Respectfully submitted,

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